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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,455	02/06/2004	Lie-Fen Shyur	08919-111001 / 14A-890529	3601

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OCCHIUTI ROHLICEK & TSAO, LLP
10 FAWCETT STREET
CAMBRIDGE, MA 02138

EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,455	SHYUR ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *2-4,6,7,9-11 and 13-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8* is/are rejected.

7)☒ Claim(s) *5 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/4/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation in part of 09/654,652, now issued as US Patent No. 7,037,696.

Claims 1-28 are pending. Claims 2-4, 6-7, 9-11 and 13-28 are withdrawn. Claims 1, 5, 8 and 12 are under consideration.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-14) with a further election of SEQ ID NO:8 in the reply filed on April 18, 2007 is acknowledged.

Claims 2-4, 6-7, 9-11, 13-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 18, 2007.

Claim for Domestic Priority

Applicants' claim to domestic priority under 35 USC 121 to US non-provisional 09/654,652, filed September 5, 2000, is acknowledged.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on May 4, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

Examiner notes that applicants have not updated the relationship of the instant application to its parent application (09/654,652) that has matured into a US patent (U.S. Patent No. 7,037,696). Examiner urges applicants to amend said information by providing the US patent number in response to this Office action.

The use of the trademarks, for example "BIOSOFT" on page 9, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Applicant's cooperation is requested in reviewing the specification for additional trademarks that may be present in the specification and making the appropriate.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 8 are drawn to a polypeptide comprising the catalytic domains of 1,3-1,4-β-D-glucanase and excluding the carboxyl terminal 78 amino acids of the 1,3-1,4-β-D-glucanase. It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In this case, the examiner has broadly interpreted the claims to encompass any polypeptides comprising any catalytic domains of any 1,3-1,4-β-D-glucanase from any or all sources, including any or all recombinants, mutants and variants of, and excluding 78 amino acids of the C-terminus. Therefore, the claims are drawn to a genus of any or all polypeptides having 1,3-1,4-β-D-glucanase activity and having any structure.

In *University of Calfornia v. Eli Lilly & Co.*, 43 USPQZd 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, (or) chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in

possession of the claimed genus. In addition, MPEP 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The recitation of "1,3-1,4-β-D-glucanase" fails to provide a sufficient description of the claimed genus of proteins as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The CAFC in UC California v. Eli Lilly, (43 USPQ2d 1398) stated that: "in claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." Similarly with the claimed genus of "1,3-1,4-β-D-glucanase" proteins, the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus.

Therefore, in the instant case, the claim is drawn to a genus of polypeptides having 1,3-1,4-β-D-glucanase activity, but having any structure. The specification only describes a polypeptide consisting of the amino acid sequence of SEQ ID NO:8, which comprises the catalytic domain the 1,3-1,4-β-D-glucanase having the amino acid sequence of SEQ ID NO:1, isolated from *Fibrobacter succinogenes,* excluding the 78 amino acids of the C-terminus. While MPEP 2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In view of the widely variant species encompassed by the genus, this one example is not enough and does not constitute a representative number of species to describe the whole genus of any or all variants, recombinant and mutants of any or all polypeptides having 1,3-1,4-β-D-glucanase activity isolated from any or all source, including any or all variants, recombinants and mutants thereof, and there is no evidence on the record of the relationship between the structure of the polypeptide of SEQ ID NO:8 and the structure of any or all recombinant, variant and mutant of any or all polypeptides having 1,3-1,4-β-D-glucanase activity. Therefore, the specification fails to describe a representative species of the genus comprising any or all polypeptides having 1,3-1,4-β-D-glucanase activity, including any or all variants, recombinants and mutants thereof.

Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention in such full,

clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of the amino acid sequence of SEQ ID NO:8, which comprises the catalytic domain the 1,3-1,4-β-D-glucanase having the amino acid sequence of SEQ ID NO:1, isolated from *Fibrobacter succinogenes,* excluding the 78 amino acids of the C-terminus, does not reasonably provide enablement for any or all polypeptides having serine protease activity isolated from any or all source, including any or all mutants, recombinants and variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1 and 8 are drawn to a polypeptide comprising the catalytic domains of 1,3-1,4-β-D-glucanase and excluding the carboxyl terminal 78 amino acids of the 1,3-1,4-β-D-glucanase.

The breadth of the claims.

It is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In this case, the examiner has broadly interpreted the claims to encompass any polypeptides comprising any catalytic domains of any 1,3-1,4-β-D-glucanase from any or all sources, including any or all recombinants, mutants and variants of, and excluding 78 amino acids of the C-terminus. Therefore, the claims are drawn to any or all polypeptides having 1,3-1,4-β-D-glucanase activity and having any structure. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of 1,3-1,4-β-D-glucanase isolated from any or all source, including any or all mutants, recombinants and variants thereof. In the instant case, the specification enables only a polypeptide consisting of the amino acid sequence of SEQ ID NO:8, which comprises the catalytic domain the 1,3-1,4-β-D-glucanase having the amino acid sequence of SEQ ID NO:1, isolated from *Fibrobacter succinogenes,* excluding the 78 amino acids of the C-terminus.

The state of prior art, the relative skill of those in the art, and predictability or unpredictability of the art.

Since the amino acid sequence of the protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In addition, the art does not provide any teaching or guidance as to (1) which amino acids within a 1,3-1,4-β-D-glucanase can be modified and which ones are conserved such that one of skill in the art can make the recited polypeptides having the same biological activity as that of the polypeptide of SEQ ID NO:8, (2) which segments of SEQ ID NO:8 or SEQ ID NO:1 are essential for activity, and (3) the general tolerance of 1,3-1,4-β-D-glucanase to structural modifications and the extent of such tolerance. The art clearly teaches that changes in a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247, 1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property

in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions.

The amount of direction or guidance presented and the existence of working examples.

The specification discloses a polypeptide consisting of the amino acid sequence of SEQ ID NO:8, which comprises the catalytic domain the 1,3-1,4-β-D-glucanase having the amino acid sequence of SEQ ID NO:1, isolated from *Fibrobacter succinogenes,* excluding the 78 amino acids of the C-terminus9. However, the speciation fails to provide any information as to (1) specific substrates associated with any 1,3-1,4-β-D-glucanase isolated from any source, including variants, mutants and recombinants thereof, (2) structural elements required in a polypeptide having 1,3-1,4-β-D-glucanase activity, or (3) which are the structural elements in a 1,3-1,4-β-D-glucanase that are essential to display 1,3-1,4-β-D-glucanase activity. No correlation between structure and function of having 1,3-1,4-β-D-glucanase activity has been presented. There is no information or guidance as to which amino acid residues in the polypeptides of SEQ ID NO:8 or SEQ ID NO:2 can be modified and which ones are to be conserved to create a polypeptide displaying the same activity as that of the polypeptides of SEQ ID NO:1.

The quantity of experimentation required to practice the claimed invention based on the teachings of the specification.

While enzyme isolation techniques, recombinant and mutagenesis techniques were known in the art at the time of the invention, e.g. hybridization or mutagenesis, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Furthermore, it is not routine in the art to create variants of polypeptides having the activity recited without any knowledge as to the structural features which would correlate with that activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all polypeptides comprising catalytic domain of a 1,3-1,4-β-D-glucanase isolated from any or all source, including variants, mutants, recombinants and fragments thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any or all mutants, variants and recombinants of any or all polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Teather et al.

Claim 1 is drawn to a polypeptide comprising the catalytic domains of 1,3-1,4-β-D-glucanase and excluding the carboxyl terminal 78 amino acids of the 1,3-1,4-β-D-glucanase.

Teather et al. (form PTO-1449) discloses a 1,3-1,4-β-D-glucanase isolated from *F. succinogenes*, wherein at least 78 amino acids at the C-terminus is deleted (page 3838, last paragraph). Therefore, the reference of Teather et al. anticipates claim 1.

Allowable Subject Matter

Claims 5 and 12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 1 and 8 are rejected.

Claims 4 and 12 are objected.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Yong D. Pak
Patent Examiner 1652